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(54) GLYCINE-CONTAINING FOOD AND USE THEREOF

(57) The present invention provides a food of the type based on unit of intake per serving, which contains glycine or a substance that can be hydrolyzed to give glycine in not less than 0.5 g based on glycine per serving. The food of the present invention can be applied as a food flavoring, a deep sleep disorder improving food or a bowel movement improving food.

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Description

Technical Field

[0001] The present invention relates to a food containing glycine and use thereof.

Background Art

[0002] Glycine is a non-essential amino acid having the simplest structure of CH_2 (NH_2) COOH. Glycine is an amino acid approved as a food additive and contained in many foods. For example, beverages contain glycine at a maximum content of about 50 mg/100 ml for the preservation of quality. In addition, glycine is also contained in fish cake products such as steamed fish paste and the like. As a known function of glycine, its intake at 0.1 g per day increases memory and attention (File. S. E. et al., Journal of Clinical Psychopharmacology, US, 1999, vol. 19, No. 6, P. 506-512). Furthermore, addition of glycine as an antispoilage agent for food together with maltose is known (JP-B-2-72853), in which case the amount of glycine to be added is, for example, about 0.3% (W/W).

Disclosure of the Invention

[0003] The present invention aims at providing a glycine-containing food of an unprecedented type, and a food having a new function based on glycine.

[0004] The present inventors have found that the intake of a given amount or more of glycine can express several unconventional new functions, and completed the present invention mentioned below.

(1) A food of the type based on unit of intake per serving, which contains glycine or a substance that can be hydrolyzed to give glycine, in an amount equivalent to not less than 0.5 g of glycine per serving.
(2) The food of the above-mentioned (1), wherein the content of the amino acid other than glycine or a substance that can be hydrolyzed to give an amino acid other than glycine is equivalent to not more than 5 g of an amino acid other than glycine per serving.
(3) The food of the above-mentioned (1) or (2), wherein the glycine or the substance that can be hydrolyzed to give glycine is a powder or a granule.
(4) The food of the above-mentioned (1) or (2), wherein the glycine or the substance that can be hydrolyzed to give glycine is slurry.
(5) The food of any of the above-mentioned (1)-(4), wherein the food is a beverage.
(6) The food of any of the above-mentioned (1)-(4), wherein the food is a confectionery.
(7) The food of any of the above-mentioned (1)-(4), wherein the food is a jelly, pudding or yoghurt.
(8) The food of the above-mentioned (1) or (2), which is used for masking a flavor of a food material itself or a flavor imparted by food processing.
(9) A food for improving a deep sleep disorder, which contains glycine or a substance that can be hydrolyzed to give glycine.
(10) A food for improving bowel movements, which contains glycine or a substance that can be hydrolyzed to give glycine.
(11) A method of masking a flavor of a food material itself or a flavor imparted by food processing, which comprises adding 0.15-100% by weight of glycine relative to the food as a whole.
(12) A method of improving a deep sleep disorder, which comprises taking a food containing glycine or a substance that can be hydrolyzed to give glycine.
(13) A method of improving bowel movements, which comprises taking a food containing glycine or a substance that can be hydrolyzed to give glycine.
(14) Use of a food containing glycine or a substance that can be hydrolyzed to give glycine for improving a deep sleep disorder.
(15) Use of a food containing glycine or a substance that can be hydrolyzed to give glycine for improving bowel movements.
(16) The food of the above-mentioned (9), which has a designation that the food is used for improving a deep sleep disorder.
(17) The food of the above-mentioned (10), which has a designation that the food is used for improving bowel movements.
(18) A commercial package comprising a food containing glycine or a substance that can be hydrolyzed to give glycine, and a written matter containing an explanation relating to use thereof for masking a flavor of a food material itself or a flavor imparted by food processing.

(19) A commercial package comprising a food containing glycine or a substance that can be hydrolyzed to give glycine, and a written matter containing an explanation relating to use thereof for improving a deep sleep disorder.
(20) A commercial package comprising a food containing glycine or a substance that can be hydrolyzed to give glycine, and a written matter containing an explanation relating to use thereof for improving bowel movements.

Brief Description of the Drawings

[0005]

Fig. 1 shows glycine intake and sleep hours during a trip to the East Coast, USA, by the test participant (Experimental Example 2).
Fig. 2 is a graph showing the relationship between the lapse of time after glycine administration and R-R interval in a test using beagles (Experimental Example 7) .

Best Mode for Carrying Out the Invention

[0006] The embodiment of the present invention is described in the following.
[0007] The subject matter of the present invention is novel use of glycine and a food suitable for the use thereof. As mentioned above, glycine is an amino acid having the structure of CH_2 (NH_2) COOH. The "substance that can be hydrolyzed to give glycine" is a substance that affords glycine by hydrolysis (particularly hydrolysis in vivo). Representative examples thereof include proteins and peptides having glycine as a constituent unit. A substance that affords glycine by hydrolysis is expected to provide the same effect as that achieved by direct glycine intake, as a result of generation of glycine due to hydrolysis in the body after the intake.
[0008] The food of the type based on unit of intake per serving in the present invention contains glycine or a substance that can be hydrolyzed to give glycine in an amount equivalent to not less than 0.5 g of glycine per serving. Since such food permits easy intake of a large amount of glycine, it allows enjoyment of effects provided by the below-mentioned novel action.
[0009] The "food of the type based on unit of intake per serving" includes foods having a predetermined amount of intake per serving. In the present specification, food is a concept broadly encompassing those that can be taken orally (excluding pharmaceutical products), and includes what is called "food", as well as beverage, health aid food, healthcare functional food, supplement and the like. The unit of intake per serving in the case of, for example, beverage, candy, chewing gum, jelly, pudding, yoghurt and the like, is a pack, a packing, a bottle and the like that define a given amount, and that in the case of a granular, powdery or slurry food is a packing and the like that define a given amount, or a container and the like that indicate the amount of intake per serving.
[0010] Being "equivalent to glycine" in relation to the content of glycine or a substance that can be hydrolyzed to give glycine in a food means that note is taken of the weight of glycine when glycine itself is contained, and when a substance that can be hydrolyzed to give glycine is contained, note is taken of the weight of glycine when the substance that can be hydrolyzed to give glycine has been entirely converted to glycine. When a food contains both glycine and a substance that can be hydrolyzed to give glycine, the total weight of glycine and a substance that can be hydrolyzed to give glycine after complete conversion to glycine by hydrolysis.
[0011] The content of glycine or a substance that can be hydrolyzed to give glycine per serving is not less than 0.5 g, preferably not less than 1.0 g, more preferably not less than 1.5 g, when converted to the amount of glycine, in view of easiness of addition to food and the effect of the addition. In addition, the above-mentioned content is preferably not more than 100 g, more preferably not more than 60 g, from eating experience based on known findings (Evins A. E. et al., American Journal of Psychiatry, US, May 2000, vol. 157, No. 5, P. 826-828) and easiness of packing and intake.
[0012] The present inventors have also found that the presence of a large amount of an amino acid other than glycine in the above-mentioned food tends to prevent the benefit of the below-mentioned effects. Therefore, the content of an amino acid other than glycine or a substance that can be hydrolyzed to give an amino acid other than glycine is preferably equivalent to not more than 5 g of an amino acid other than glycine per serving. When the amount of an amino acid other than glycine and a substance that can be hydrolyzed to give an amino acid other than glycine exceeds 5 g in the above-mentioned food containing glycine at a lowest level permitting functional expression, the function of glycine in the present invention is suppressed.
[0013] While the lower limit of the content of an amino acids other than glycine or a substance that can be hydrolyzed to give an amino acid other than glycine is not particularly defined, for example, 50 mg per serving of an amino acid other than glycine can be mentioned, with preference given to substantial absence.
[0014] The amino acid other than glycine refers to amino acid other than the above-mentioned glycine. As used herein, by the "amino acid" is meant an organic compound having both an amino group (-NH_2) and a carboxyl group (-COOH). The "substance that can be hydrolyzed to give an amino acid other than glycine" is a substance affording

an organic compound (except for glycine) having both an amino group and a carboxyl group by hydrolysis (particularly hydrolysis in vivo), and typical examples include proteins and peptides having an amino acid other than glycine as a constituent element can be mentioned.

[0015] Being "equivalent to an amino acid other than glycine" in relation to the content of an amino acid other than glycine or a substance that can be hydrolyzed to give an amino acid other than glycine in a food means that note is taken of the total of the weight of an amino acid other than glycine and the weight of an amino acid other than glycine, assuming that a substance that can be hydrolyzed to give an amino acid other than glycine has become an amino acid other than glycine by hydrolysis.

[0016] The shape of the glycine or a substance that can be hydrolyzed to give glycine contained in a food is not particularly limited and may be a powder or granule, as well as slurry, tablet, capsule, solution, gel or emulsion. Of these, granules and powder are preferable for portability and easiness of packing. In addition, solution, gel and slurry are also preferable because of the easiness of intake.

[0017] The "slurry" glycine contained in food means a state where solid glycine is suspended in a liquid media. A part of glycine may be dissolved in the above-mentioned media.

[0018] For example, when the food is what is called a health food, not less than 0.5 g of granular glycine may be packed in an intake unit amount and the like. When the food is a healthy drink, for example, a drink containing not less than 0.5 g of glycine in a suspension or solution is placed in a bottle etc. sized for one meal.

[0019] The type of food is not particularly limited and application to various foods is possible. Since glycine has high solubility in water and has preferable sweetness, it can be suitably applied to beverage, confectionery, jelly, pudding or yoghurt. Beverages may be served in a bottle, a can, a paper pack and the like in the form of a solution, a suspension and the like, or may be extracted or dissolved for drinking like tea, coffee, powder beverage and the like. As used herein, by the confectionery is meant favorite food taken besides meals, such as sweets and the like (e.g., candy, chewing gum, tablet and the like).

[0020] As the animals other than human to be administered to, mammals such as domestic animal, fowl and the like, experimental animals and the like can be mentioned. The mode of administration to animals other than human may be addition to diet.

[0021] The invention relating to the novel use of glycine is explained in the following. The novel use of the present invention refers to use as food flavoring, arousal during sleep and early-morning awakening suppressing food, deep sleep disorder improving food or bowel movement improving food.

<Food flavoring>

[0022] Conventionally, amino acids have been generally used as a reaction flavor under special conditions of industrial environment at high temperature. The present inventors have found that a preferable flavor can be produced upon reaction with sugars contained in the food under conditions that can be generally produced at home, such as addition of boiled water to glycine and the like. In addition, they have found that glycine can be used for masking of undesirable flavor in the food.

[0023] The food flavoring in the present invention is a concept expressing a substance that adds flavor to a food material having almost no flavor, enforcing the flavor lost during production of food, masking an unpreferable flavor a food material itself has or produced during processing.

[0024] For use as a food flavoring, glycine only needs to be added to a food. The glycine content can be appropriately determined according to the amount of the flavor to be added and the level of masking to be performed. In the case of a food of the type based on the unit of intake per serving, glycine is added in an amount of preferably 0.5-100 g, more preferably 1.0-60 g, per serving. In addition, the weight of glycine in the whole food is preferably 0.15-100 wt%, more preferably 0.3-98 wt%, in consideration of solubility, preferable taste, and effectiveness of flavor and masking. A preferable mode of use for this purpose is, for example, allowing reaction with sugars by heating, such as addition of boiling water and the like. In this case, as the sugars to be reacted, sucrose, fructose, glucose, dextrin, maltose and the like can be mentioned.

[0025] The present invention also encompasses a method of masking a flavor of a food material itself or a flavor imparted by food processing, which comprises adding glycine in a proportion of 0.15-100% by weight, preferably 0.3-98 wt%, of the whole food.

[0026] The "unpreferable flavor" in a food for which glycine is used for masking includes flavors of medicinal plants used for crude drug and Chinese herbal medicine, yacon, Eucommia ulmoides and Puer contained in general health food and the like, plant extracts such as Houttuynia cordata used for folk remedy and the like, and herbs generally taken as herb or extracted for drinking.

<Deep sleep disorder improving food>

[0027] Another aspect of the present invention is use of a food containing glycine (or a substance that can be hydrolyzed to give glycine) as a deep sleep disorder improving food.

[0028] As used herein, by the "deep sleep disorder" is meant a condition lacking satisfaction from deep sleep on awakening, or a condition of shortage of sleep, or a condition lacking satisfaction in various aspects expected to be afforded by a suitable sleep. For example, such condition includes shallow sleep, difficult shift to slow wave sleep indicating profound sleep after sleep onset, interrupted sleep, failure to get up at expected time and insufficient sleep hours, and is considered to often occur in an unsuitable sleep environment, in the presence of mental or physical stress, after intake of an ingredient having an awakening effect such as caffeine and the like before bedtime, at the time of excessive drinking, irregular sleep cycles and disturbed biological rhythm, as well as in a time lag environment. It is generally known that sleep plays a role of resting the body, as well as more positively relieving physical and mental fatigue, organizing the memory, and particularly in deep sleep, controlling growth and metabolism balance in the body by the secretion of growth hormone etc. Therefore, when physical or mental condition is not improved, fatigue remains, enthusiasm in life is diminished, oversleep occurs the next day, feel lethargic, feel shortage of sleep hours, or a headache occurs after sleeping due to a deep sleep disorder, improvement of these (improvement of deep sleep disorder) is expected to result in, for example, improved physical or mental conditions as shown by decreased lassitude, pleasant awakening on rising and the like, and realization of deep sleep, realization of fine sleep, which in turn increases willingness in life, concentration and the like. In addition, irregular work accompanying shift work and the like, moving with a jet lag and the like can also cause a deep sleep disorder, and improvement of these is expected to increase concentration during waking time, prevent oversleep during the daytime, decrease lassitude, and increase willingness to work. A deep sleep disorder improving food is effective not only for improving the above-mentioned deep sleep disorder but also allowing the inherent role of sleep to be fulfilled by improving the quality of sleep. Such a role includes, for example, affording the feeling of being refreshed on rising, decreasing lassitude, preventing tendency of oversleeping during the daytime and the like. A deep sleep disorder improving food can improve the above-mentioned deep sleep disorders. The concept represented by what is called a "sleep disorder" and "insomnia" is also included in the concept of the aforementioned "deep sleep disorder".

[0029] The food of the present invention as a deep sleep disorder improving food contains glycine or a substance that can be hydrolyzed to give glycine. The amount of intake of the aforementioned food for this purpose is preferably 0.00625-2.5 g/kg/day, more preferably 0.125-1.5 g/kg/day (daily intake per 1 kg of body weight), in an amount equivalent to glycine. The "equivalent to glycine" means as mentioned above. An amount not less than the lower limit of the aforementioned numerical range is sufficient to afford the aforementioned effect. When the amount of intake is increased, the intake tends to be come difficult, and the cost becomes high. A food of the aforementioned type based on the unit of intake per serving facilitates control of the amount of intake of glycine.

[0030] By the aforementioned effect relating to sleep, suppression of sleepiness during the daytime, particularly, enhanced quality of sleep in an environment associated with time difference such as jet lag and the like is expected. The life nowadays sometimes makes it difficult to ensure regular sleep because of the shift of life hours, rotation work and the like. In an environment of inconsistent life time pattern as the above, the quality of life can be improved by increasing the realization of deep sleep on waking and less sleepiness during daytime. While the effect of glycine as mentioned above is assumed to be related to several mechanisms, an action on the sympathetic and parasympathetic nervous system is considered to be particularly significant. The results in a test involving measurement of electrocardiogram of experimental animals indicate that administration of glycine dominantly acts on the parasympathetic nervous system. It is said that the present-day life tends to be sympathetic dominant due to mental stress and the like. Glycine is considered to induce shift to slow wave sleep (deep sleep), improves the quality of sleep during sleep hours, appropriately controls visceral activity during sleep and encourages natural sleep by allowing dominant action on parasympathetic that acts opposite to sympathetic dominant. When glycine is taken for such use relating to sleep, it is most suitably taken before going to bed.

[0031] As a lower concept of the deep sleep disorder improving food, an arousal during sleep suppressing food and an early-morning awakening suppressing food can be mentioned. As used herein, by the "arousal during sleep" is meant waking up at night and being unable to go back to sleep for a while thereafter and by the "early-morning awakening" is meant waking up earlier than intended and being unable to go back to sleep again. An arousal during sleep or early-morning awakening suppressing food can improve at least one condition of the above-mentioned arousal during sleep and early-morning awakening.

[0032] The food of the present invention as an arousal during sleep or early-morning awakening suppressing food contains glycine or a substance that can be hydrolyzed to give glycine. The preferable amount of intake of the aforementioned food for this purpose is the same as that of a deep sleep disorder improving food.

<Bowel movement improving food>

[0033] Another embodiment of the present invention is use of a food containing glycine (or a substance that can be hydrolyzed to give glycine) as a bowel movement improving food. As used herein, by the "bowel movement improving" is meant a food capable of improving abnormal bowel movements (i.e., constipation and diarrhea).

[0034] For use as a bowel movement improving food, a food containing glycine or a substance that can be hydrolyzed to give glycine only needs to be taken. The preferable amount of intake of the aforementioned food for this purpose is the same as that of a deep sleep disorder improving food.

<Commercial package>

[0035] In a package containing the food of the present invention and a written matter with an explanation relating to the use thereof, the written matter is, for example, what is called a package insert describing items relating to use, efficacy, drinking/eating method etc., and the like.

Examples

[0036] The present invention is explained in detail by referring to examples. The examples are mere exemplifications and do not limit the present invention in any way. In the tests in Experimental Examples 1-6, 8 other than the test using experimental animals, all test participants voluntarily took glycine as a food additive based on his or her independent wish as a powder or tablet or upon addition to general food, and made comments by his or her free will, which are summarized in those examples. The tests of Experimental Example 9 and the following were performed by a double-blind placebo study upon approval of internal ethical review board and under direction of specialized physician.

(Experimental Example 1)

[0037] Glycine powder (substantially pure, 2 g) was added to commercially available tea bags of the blend tea shown in Table 1 and the same tea bags without the addition were also prepared. A given amount (150 mL) of hot water was added and the tea was extracted for 1 min. Five test participants drank the extracted blend tea and commented as to the decrease of flavor by the addition of glycine as compared to non-addition of glycine. The decrease of flavor was taken as an index of the masking effect (Table 1). The majority of the test participants confirmed the masking effect in all three kinds of the tested blend tea, and most of them found it to be a preferable masking effect.

Table 1

Masking effect by addition of 2 g of glycine per serving to food (unit: person)			
Added to	Masking effect present		No masking effect
	Preferable effect	Unpreferable effect	
Pure blend tea	1	2	2
Eucommia ulmoides blend tea	4	0	1
Korean ginseng blend tea	3	0	2

(Experimental Example 2)

[0038] The glycine intake and sleep hours when a Japanese test participant living in Japan (male, 44 years old, body weight 62 kg) traveled to the East Coast, USA, are shown in Fig. 1. In the Figure, glycine (substantially pure tablet glycine containing only excipient and flavor) was taken at the time point marked with an arrow, wherein 1.0 g was taken on "June 20" and "June 21" and 1.5 g was taken on "June 22" - "June 26" and "June 29". This test participant frequently woke up during sleep in previous similar trips, but as is clear from the results of Fig. 1, administration of glycine reduced or eliminated arousal during sleep.

(Experimental Example 3)

[0039] Three test participants (test participants A-C, body weight 64-74 kg) who were then visiting US for 5 days took glycine (1.5 g, substantially pure tablet glycine containing only excipient and flavor) before sleep and evaluated sleepiness felt from 1 pm to 5 pm the next afternoon in 3 levels as compared to the absence of glycine. The results

are summarized in Table 2. All three test participants felt lower level of sleepiness during the next daytime by the intake of glycine as compared to the absence of glycine.

Table 2

Reduction of sleepiness during daytime the next day due to the intake of glycine in environment with time difference (unit: day)				
		No sleepiness	Mild sleepiness	Heavy sleepiness
Test participant A	Intake of glycine	2	2	0
	Without intake of glycine	0	0	1
Test participant B	Intake of glycine	2	1	0
	Without intake of glycine	0	0	2
Test participant C	Intake of glycine	1	0	0
	Without intake of glycine	0	2	2

(Experimental Example 4)

[0040] The test participant (body weight 45 kg) took, before going to bed, 3 g of glycine directly or upon addition to various foods (see Table 3). The content (amount based on amino acid) of an amino acid other than glycine or a substance that can be hydrolyzed to give an amino acid other than glycine in these foods was generally 0-4 g. As compared to free of glycine intake, easiness of falling asleep and realization of deep sleep upon waking the next morning were recorded and summarized in Table 3. By any form of glycine intake, realization of deep sleep and easiness of falling asleep were improved in most cases.

Table 3

Improvement of realization of deep sleep and easiness of falling asleep by glycine (3 g) intake before going to bed (unit: day)			
Food containing glycine	Days of testing	Improved realization of deep sleep	Improved easiness of falling asleep
Powder	3	3	3
Addition to hot milk	4	4	4
Addition to yoghurt	7	7	7
Addition to herb tea	5	5	5
Addition to Japanese tea	10	10	9
Addition to hot water or water	14	14	14

(Experimental Example 5)

[0041] The test participants (body weight 45-80 kg) took 3 g of glycine (substantially pure glycine granule and powder) as it was, or after dissolving or suspending in water, juice, sport beverage and the like, or after addition to jelly, pudding and the like and then slept, after which they voluntarily commented on the quality of sleep as compared to the absence of intake. Out of 77 participants, 58 participants commented that the quality of sleep was improved, 2 participants commented that the quality was degraded and 17 participants commented that no effect was found. The effects on waking such as freshness on waking and improved realization of deep sleep, as well as the effect on the next day of the intake such as reduced sleepiness during daytime, and the effect after the intake such as reduced snore during sleep were found. Besides the above, the minority of participants commented that the stomach ache was reduced, fatigue did not remain the next morning, the mental stress before examination was reduced, menstrual pain became mild, oversleep ceased, stuffed nose was solved and the like (see Table 4).

Table 4

Effect on quality of sleep by glycine (3 g) intake (voluntary comments of 77 participants, unit: person)		
	Enhancing effect on quality of sleep	Degrading effect
Awakening was fresh	24	1
Sleep was deeper	10	0
Deep sleep was realized	8	0
Had no dream	4	0
Slept well	2	0
Did not wake up at midnight	6	1
Fell asleep easily	6	0
Sleepiness during daytime reduced	4	0
Snore decreased	19	0

(Experimental Example 6)

[0042] Two test participants (test participant A (body weight 52 kg), B (body weight 45 kg)) took or did not take, before going to bed, glycine (substantially pure tablet glycine containing only excipient and flavor) of the type shown in Table 5. Table 5 shows bowel movements in the next morning and the corresponding number of days. When glycine was taken before going to bed, the bowel movements in the next morning increased. When taken together with yoghurt, the bowel movements were also improved.

Table 5

Improved bowel movements by glycine intake (unit: day)			
		Presence of bowel movement	No bowel movement
Test participant A	Tablet intake (1 g)	10	2
	No intake	4	6
Test participant B	Powder intake (3 g)	7	1
	Intake (3 g) with yoghurt	4	0
	Only yoghurt	3	2
	No intake	2	3

(Experimental Example 7)

[0043] Glycine (substantially pure glycine powder) was administered at 0, 30, 300 mg/kg (0 mg/kg for control, CTRL) to beagles and using the beagles, R-R interval in electrocardiogram to be an index of sympathetic activity was measured by a telemetry system. The measurement was conducted in the night after glycine administration. From R-R interval after oral administration of glycine, moreover, sympathetic activity ([low frequency component LF]/[high frequency component HF]) and parasympathetic activity (high frequency component HF) were examined by fast Fourier transform power spectrum analysis. Fig. 2 shows the relationship between the lapse of time after administration and R-R interval. As a result, it was found that R-R interval increased at 1-4 hr after administration as compared to the control, and the parasympathetic activity was dominant. The results suggest possible involvement of glycine in the relaxation of deep sleep disorders by the relative suppression of sympathetic hyperactivity.

(Experimental Example 8)

[0044] The test participant A (body weight 45 kg) took glycine (substantially pure powder) in an amount shown in Table 6 before going to bed by dissolving same in water, and recorded the level of realization of deep sleep. When the realization of deep sleep increased than usual, "+" was marked, when the realization of deep sleep was almost the

same as usual, "±" was marked and when it became worse, "-" was marked. The results are shown in Table 6.

Table 6

Amount of intake (in teaspoon)	1/4	1/2	1/1
General amount (g)	0.6	1.2	2.5
Realization of deep sleep	+	+	+

(Experimental Example 9)

[0045] A double-blind crossover test aiming at confirmation of the effect of glycine on sleep was performed with 15 female adults (20s - 50s, body weight 46-58 kg). The test participants took glycine (granule containing citric acid and the like) in an amount equivalent to 3 g of glycine 1 hr before bedtime, and reduced maltose containing components other than glycine (citric acid and the like) and adjusted to an almost indistinguishable taste was used as a placebo. For the test, glycine and placebo were each taken for 4 days with an interval of a 3 day non-intake period, totaling 2 weeks.

(1) As a result of examination using self recording questionnaire for the evaluation of sleep condition, the test participants of 32 years old or older (6 out of 15 participants, body weight 46-58 kg) significantly showed an effect of improving physical conditions on waking (good physical shape, lethargic feeling, heavy-headed feeling and the like) and mental conditions on waking (refreshed feeling, sick feeling and the like), and the test participant having problems regarding sleep (7 out of 15 participants, body weight 46-58 kg) who marked 9 points or more in the Pittsburgh Sleep Quality Index (PSQI) significantly showed an effect of improving mental conditions on waking. The results are shown in Table 7.

Table 7

Improvement of physical and mental conditions on waking by glycine intake (unit: person)			
Evaluation item	Comparison with placebo	32 years old or older	PSQI not less than 9
Physical condition on waking	Improved	5	5
	No change	1	1
	Worsened	0	1
Mental condition on waking	Improved	5	5
	No change	1	2
	Worsened	0	0

(2) As a result of examination using self recording questionnaire for the evaluation of lassitude on waking, a tendency of reducing lassitude on waking was observed. The results are shown in Table 8. In the Table, the values of glycine and placebo show the number of test participants who showed decrease of lassitude (decreased total point) or increase (increased total point) as compared to placebo intake, in the total point of 4 days of 10 questions (each 3 levels of 0, 1, 2 points) evaluating the lassitude on waking in a SAM lassitude check list. In the Table, the number of test participants who showed difference by 1 point or more (effective) in the total points and who showed difference by 4 points or more (remarkably effective) are shown.

Table 8

Effect of reducing lassitude on waking by glycine intake		
	Effective	Remarkably effective
Reduction of lassitude (participants)	11	7
No change (participants)	1	6
Increase of lassitude (participants)	3	2

(3) As a result of examination using self recording questionnaire for the evaluation of sleep condition, the test participants of 32 years old or older showed significant effect of improving the depth of sleep. The results are

shown in Table 9. In the Table, the values of glycine and placebo show the test participant average of the points of evaluation in 8 levels in the sleep questionnaire "depth of sleep". A greater numerical value indicates that the test participant felt deeper sleep. In addition, p value is a statistical value showing the probability when the difference between glycine and placebo was hypothesized to be null. Particularly, this value of 0.05 or below is considered to indicate a significant difference.

Table 9

Effect of improving depth of sleep by glycine intake			
	Glycine	Placebo	p value
Sleep questionnaire "depth of sleep"	4.88	4.13	0.042

(4) At the end of each 1 week test period, a question was asked about the sound sleep. As a result 6 out of 15 participants answered that the week of glycine intake was fine and one participant answered that the week of placebo intake was fine. The remaining 8 participants answered that both were the same.
(5) As a result of examination using self recording questionnaire for the evaluation of sleep condition, the test participants of 32 years old or older particularly showed an effect of clearing head the next morning. The results are summarized in Table 10.

Table 10

Effect of clearing head the next morning by glycine intake (unit: person)		
	Comparison with placebo	Number of participants
Effect of clearing head the next morning	Effective	5
	No change	1
	Worsened	0

[0046] From the above, it has been shown that glycine intake affords deep sleep, and improves lassitude on waking and physical or mental condition. It is assumed that, as a result of the deep sleep, fatigue was eliminated and the condition on waking was improved.

(Experimental Example 10)

[0047] A double-blind crossover test aiming at confirmation of the effect of glycine on sleep was performed with 14 male adults (body weight 64-112.5 kg, average 81.2 kg) concerned about snoring and apnea condition during sleep. The test participants took glycine (granule containing citric acid and the like) in an amount equivalent to 3 g of glycine 1 hr before bedtime, and reduced maltose containing components other than glycine (citric acid and the like) and adjusted to an almost indistinguishable taste was used as a placebo.

(1) For the evaluation of sleep condition, overnight polysomnography was used for the measurement. As a result, significant difference was not observed in the time from lights-out to sleep onset, but the time from the lights-out to slow wave sleep considered to represent deep sleep was shortened and extension of the slow wave sleep in the early stage of sleep onset was confirmed.

In addition, the sleep condition of the night before was examined on waking using the sleep questionnaire. As a result, high marks were obtained for the item of "depth of sleep". This suggests that the glycine intake facilitated deep sleep. The results are summarized in Table 11. The slow wave sleep (%) in early stage of sleep onset in the Table shows a test participant average of the ratio of slow wave sleep to the early stage (1 hr) of sleep onset.

In the OSA sleep questionnaire, a test participant average of the points of 4 levels (0, 11, 21, 32 points) was calculated. A higher points means the answer of the test participant that the sleep was deeper. The point with the glycine intake was 16.7, which is higher than the point 12.3 with placebo intake. This means deeper sleep afforded by the glycine intake.

Table 11

Effect of facilitating deep sleep by glycine intake			
	Glycine	Placebo	p value
Lights-out - sleep onset (min.)	13.3	16.3	0.322
Lights-out - slow wave sleep (min.)	52.2	103.4	0.042
Slow wave sleep (%) in sleep onset initial stage	12.0	6.4	0.020

(2) The sleep condition of the night before was examined on waking using the OSA sleep questionnaire. As a result, the tendency of less time of dozing off was obtained. It is considered that resistance to sleep onset during bedtime was reduced. In the OSA sleep questionnaire, a test participant average of the points of 4 levels (0, 11, 19, 30 points) was calculated. A higher points means the answer of the test participant that the time of dozing off was shorter. The point with the glycine intake was 24.9, which is higher than the point 19.6 with placebo intake. This means that the time of dozing off was shorter by the glycine intake and deep sleep was obtained after the sleep onset.

(Experimental Example 11)

[0048] Glycine (substantially pure glycine powder) was administered to rats at 0 g/kg and 2 g/kg (0 g/kg for control) and using the rat, spontaneous electroencephalogram and cervix electromyogram were recorded through an electrode placed in the cortex. hippocampus, and further, the amount of spontaneous motor activity was measured by an infrared ray monitor. The sleep-wake cycle was analyzed from the electroencephalogram, electromyogram and behavior record (kymogram), and percent occupation of light period and dark period and latency time were calculated. Table 12 shows percent occupation of sleep-wake cycle at every 3 hours, Table 13 shows latency time and Table 14 shows the amount of spontaneous motor activity at 6 hours after administration (all in mean±standard error).

Table 12

Percent occupation of each sleep - wake cycle (unit:%) after administration			
Sleep - wake cycle	Lapse of time (hr) after administration	Light period	Dark period
		Control group Glycine group	Control group Glycine group
Waking stage	0-3	44.4±7.1 39.6±6.0	71.6±4.1 67.6±7.9
	4-6	32.4±1.3 20.7±0.8	69.3±1.3 65.6±3.4
Slow wave sleep stage	0-3	49.6±6.1 54.9±4.9	25.7±3.6 29.2±6.5
	4-6	56.1±1.9 65.9±2.0	28.3±1.4 31.5±2.8
Fast wave sleep stage	0-3	6.0±1.7 5.5±1.6	2.7±0.9 3.2±1.7
	4-6	11.5±1.3 13.4±2.1	2.4±0.4 3.0±0.7

Table 13

Latency time (unit: min) of each sleep stage after administration				
Sleep - wake cycle	Light period		Dark period	
	Control group	Glycine group	Control group	Glycine group
Slow wave sleep stage	22.1± 9	8.5±1.2	73.0±13.4	78.6±22.8
Fast wave sleep stage	20.4± 6	20.9±3.4	99.6±34.6	118.2±28.3

Table 14

Amount (unit: count) of spontaneous motor activity at 6 hr after administration		
	Control group	Glycine group
Light period	4193± 777	2316± 295
Dark period	21519±2997	19464±2765

[0049] When glycine was administered during the daytime, the proportion of waking stage became less as compared to the control. As to the detail of the sleep stage, both the slow wave sleep stage and the fast wave sleep stage slightly increased. In contrast, the dark period did not show any effect. As shown in Table 13, for each latency time of the sleep stage, namely, the time before the first emergence of sleep after administration, the slow wave sleep stage latency time was shortened in the glycine administration group and it was suggested that a deep sleep might have been easily induced by glycine.

[0050] As shown in Table 14, moreover, the amount of spontaneous motor activity during the light period decreased in the glycine administration group, but it did not show any difference in the dark period. From the above results, it was shown that glycine encourages natural sleep without markedly changing the constitution of sleep only in the light period, which is the inherent resting stage of rats.

Industrial Applicability

[0051] The food of the present invention can provide an unpreferable flavor masking effect, a deep sleep disorder improving effect, such as an arousal during sleep suppressing effect and an early-morning awakening suppressing effect, a bowel movement improving effect and the like. A food of the type based on the unit intake of the present invention can easily enjoy the effect afforded by the above-mentioned action.

[0052] This application is based on application Nos. 2004-007392 and 2004-158917 filed in Japan, the contents of which are incorporated hereinto by reference.

Claims

1. A food of the type based on unit of intake per serving, which contains glycine or a substance that can be hydrolyzed to give glycine, in an amount equivalent to not less than 0.5 g of glycine per serving.

2. The food of claim 1, wherein the content of the amino acid other than glycine or a substance that can be hydrolyzed to give an amino acid other than glycine is equivalent to not more than 5 g of an amino acid other than glycine per serving.

3. The food of claim 1 or 2, wherein the glycine or the substance that can be hydrolyzed to give glycine is a powder or a granule.

4. The food of claim 1 or 2, wherein the glycine or the substance that can be hydrolyzed to give glycine is slurry.

5. The food of any of claims 1 to 4, wherein the food is a beverage.

6. The food of any of claims 1 to 4, wherein the food is a confectionery.

7. The food of any of claims 1 to 4, wherein the food is a jelly, pudding or yoghurt.

8. The food of claim 1 or 2, which is used for masking a flavor of a food material itself or a flavor imparted by food processing.

9. A food for improving a deep sleep disorder, which contains glycine or a substance that can be hydrolyzed to give glycine.

10. A food for improving bowel movements, which contains glycine or a substance that can be hydrolyzed to give glycine.

11. A method of masking a flavor of a food material itself or a flavor imparted by food processing, which comprises adding 0.15-100% by weight of glycine relative to the food as a whole.

12. A method of improving a deep sleep disorder, which comprises taking a food containing glycine or a substance that can be hydrolyzed to give glycine.

13. A method of improving bowel movements, which comprises taking a food containing glycine or a substance that can be hydrolyzed to give glycine.

14. Use of a food containing glycine or a substance that can be hydrolyzed to give glycine for improving a deep sleep disorder.

15. Use of a food containing glycine or a substance that can be hydrolyzed to give glycine for improving bowel movements.

16. The food of claim 9, which has a designation that the food is used for improving a deep sleep disorder.

17. The food of claim 10, which has a designation that the food is used for improving bowel movements.

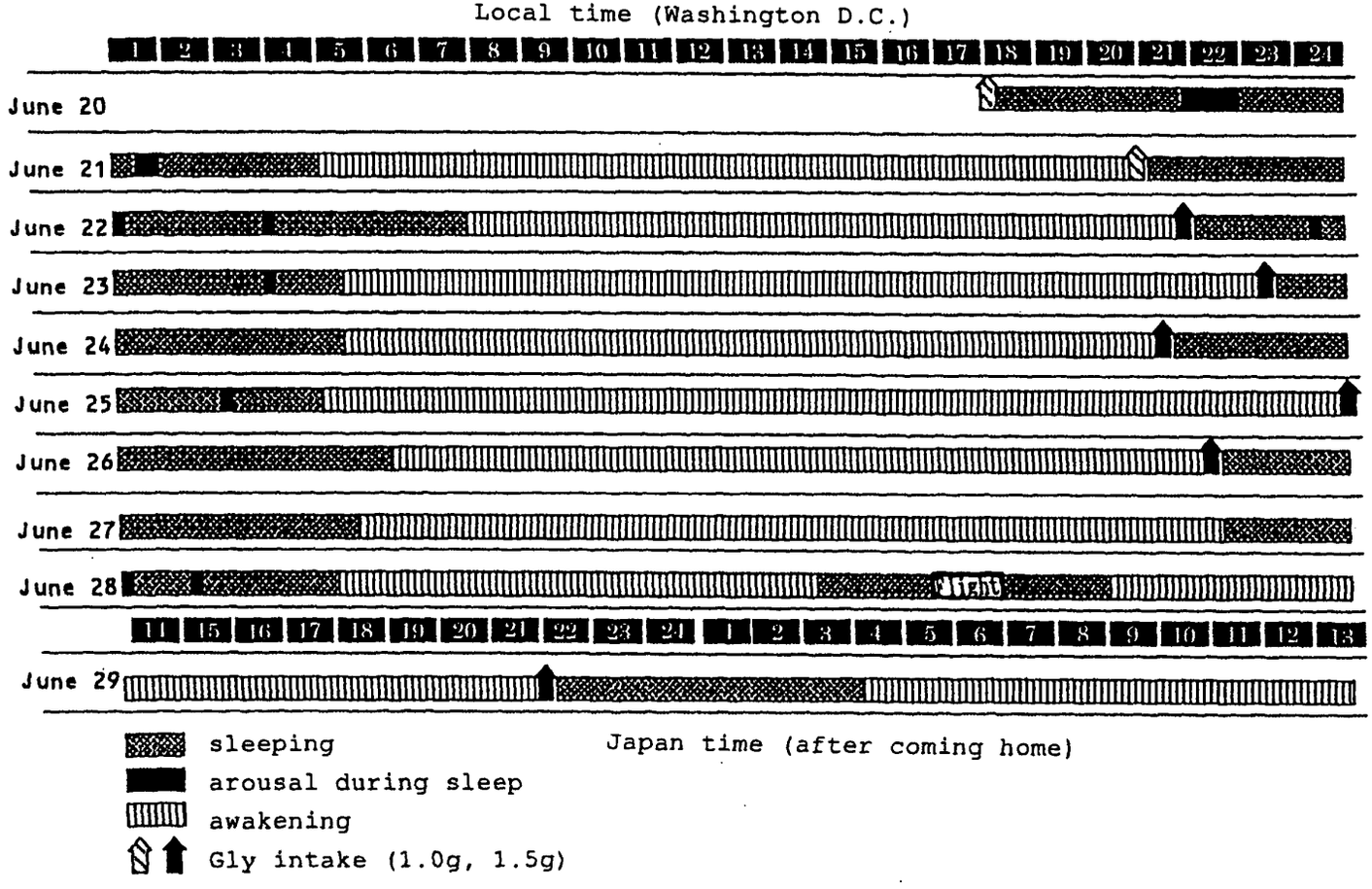
18. A commercial package comprising a food containing glycine or a substance that can be hydrolyzed to give glycine, and a written matter containing an explanation relating to use thereof for masking a flavor of a food material itself or a flavor imparted by food processing.

19. A commercial package comprising a food containing glycine or a substance that can be hydrolyzed to give glycine, and a written matter containing an explanation relating to use thereof for improving a deep sleep disorder.

20. A commercial package comprising a food containing glycine or a substance that can be hydrolyzed to give glycine, and a written matter containing an explanation relating to use thereof for improving bowel movements.

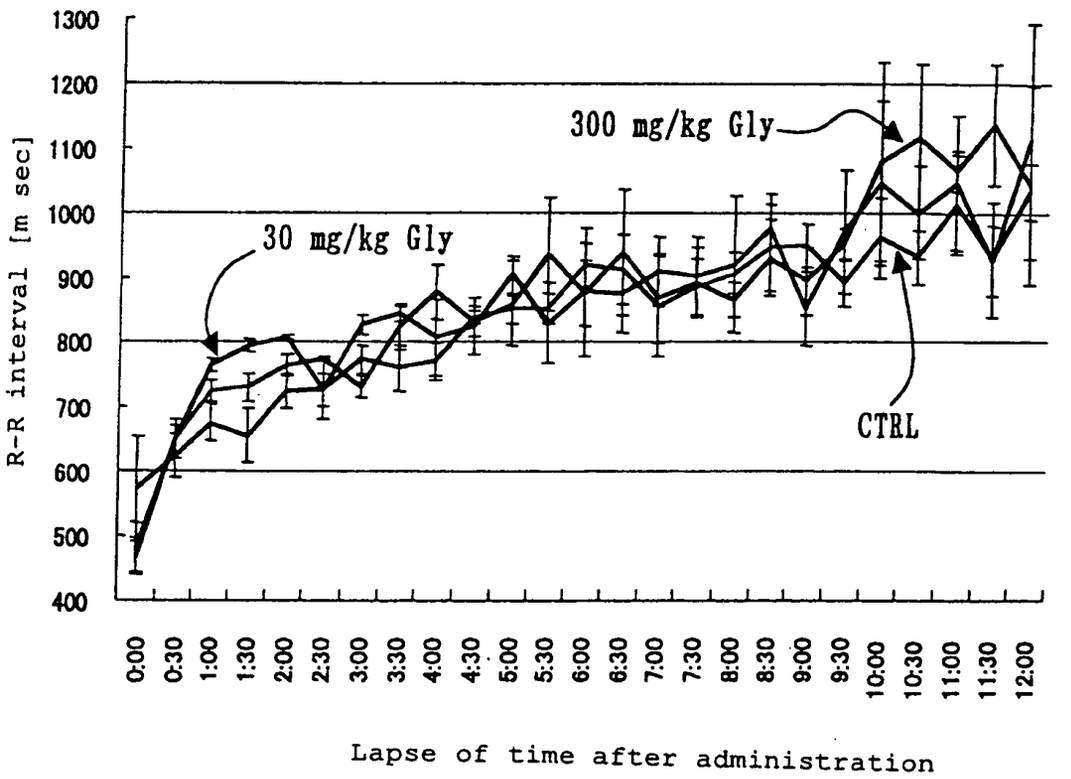
FIG. 1

Effect of glycine intake in the environment associated with jet lag



EP 1 609 375 A1

FIG. 2


1300
1200
1100
1000
900
800
700
600
500
400
R-R interval [m sec]
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30 mg/kg Gly
CTRL
0:00
0:30
1:00
1:30
2:00
2:30
3:00
3:30
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6:30
7:00
7:30
8:00
8:30
9:00
9:30
10:00
10:30
11:00
11:30
12:00
Lapse of time after administration

INTERNATIONAL SEARCH REPORT

International application No.
PCT/JP2004/019771

A. CLASSIFICATION OF SUBJECT MATTER
Int.Cl[7] A23L1/305, A23L2/00, A23L1/015

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
Int.Cl[7] A23L1/305, A23L2/00-2/52, A61K31/198

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
JSTPlus(JOIS)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	JP 4-207161 A (Rohto Pharmaceutical Co., Ltd.), 29 July, 1992 (29.07.92), (Family: none)	1-11,16-20
X	Satoshi TERASAKI, "Glycine no Riyo to sono Koka", Food Processing, 1992, Vol.27, No.10, pages 11 to 14	8,11,18
X	JP 6-505014 A (KOMISSAROVA, Irina Alexeevna), 09 June, 1994 (09.06.94), & WO 9313764 A1 & EP 575613 A1 & CN 1074134 A & US 5643954 A	9,16,19

☐ Further documents are listed in the continuation of Box C. ☐ See patent family annex.

* Special categories of cited documents:
"A" document defining the general state of the art which is not considered to be of particular relevance
"E" earlier application or patent but published on or after the international filing date
"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
"O" document referring to an oral disclosure, use, exhibition or other means
"P" document published prior to the international filing date but later than the priority date claimed
"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
30 March, 2005 (30.03.05)	19 April, 2005 (19.04.05)
Name and mailing address of the ISA/ Japanese Patent Office Facsimile No.	Authorized officer Telephone No.

Form PCT/ISA/210 (second sheet) (January 2004)

INTERNATIONAL SEARCH REPORT

International application No.
PCT/JP2004/019771

Box No. II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. [X] Claims Nos.: 12-15
because they relate to subject matter not required to be searched by this Authority, namely:
Claims 12 to 15 are practically relevant to methods for treatment of the human body by therapy and thus relate to a subject matter which this International Searching Authority is not required, under the provisions of Article 17(2)(a)(i) of the PCT (continued to extra sheet)

2. [ ] Claims Nos.:
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:

3. [ ] Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box No. III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:
The matter common to claims 1 to 8, {9, 12, 14, 16, 19}, {10, 13, 15, 17, 20} and {11, 18} resides in adding glycine to a food. However, a food containing glycine has been publicly known, as reported in, for example, JP 4-207161 A and JP 8-256685 A. Thus, this point cannot be considered as a technical feature making a contribution over prior art.
Such being the case, claims 1 to 20 have no special technical feature in common and, therefore, these groups of inventions are not considered as relating to a group of inventions so linked as to form a single general inventive concept.

1. [X] As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.

2. [ ] As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.

3. [ ] As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:

4. [ ] No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

[ ] The additional search fees were accompanied by the applicant's protest.

[X] No protest accompanied the payment of additional search fees.

Form PCT/ISA/210 (continuation of first sheet (2)) (January 2004)

INTERNATIONAL SEARCH REPORT

International application No.
PCT/JP2004/019771

Continuation of Box No.II-1 of continuation of first sheet(2)

and Rule 39.1(iv) of the Regulations under the PCT, to search.

Form PCT/ISA/210 (extra sheet) (January 2004)